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/The Cell In Its Living State/

Irritation

I am inclined to place all carcinogenic agents in one broad category of irritation. Vaky Menkin defines an irritant as "any foreign agent which interrupts the normal metabolic processes in the cell organization." It must be emphasized that mere chronic irritation of an irritant does not convert a normal cell of adult complexity to a dividing cell but produces a sequence of changes which end in the production of cancer.

Since the skin has been the object of both clinical & experimental observation & the mechanism of the cancer process it may be used as an illustration.

The dilator substances relax capillaries, veins, and arterioles and permit escape of intracellular proteins, water, minerals, androgenic or estrogenic hormones, purine and pyrimidine bases, etc. causing a swelling. This swelling may attract secondary invaders to produce the inflammatory tumors or the irritant may permit the escape of some of the tumor cells of isolation 'or cell rests' whose character is universal migration to enter this changed environment of swelling. These cells mix their embryonal potencies, assimilate the chemical components of their environment and then divide into mother cells and daughter cells. The daughter cells grow according to their kind, attract and attach each other because of their character of stickiness to form a new growth or they may enter an environment of predetermined selectivity where like cells attract/like cells to become carcinoma or sarcoma.

SENESCENCE

H.G.Bray and K. White discuss growth and aging in Organisms as Physico Chemical Machines saying "It is well known that during growth the intake of material by an organism exceeds the output and that when it is mature these processes are balanced. Thus in terms of our discussion in this article we may say that the growing organism is an open system approaching a steady state. Growth ceases with the attainment of adulthood but, in a strict sense, a true steady state is never achieved, but is approached more and more slowly as life proceeds. This may be seen in the gradual decrease in basal metabolism and in other physiological characteristics which change with age."

Thus every cell, tissue or organ may have its particular response in a gradual decrease in basal metabolism and in other physiological character-

permitting the escape of some of these isolated cells which continue to grow according to their kind to occupy passages suddenly & abruptly to interfere & function, to cause ulcerations, erosion, perforation & hemorrhage & thereby even life itself.

available to perform work. Gluco-6-phosphate is not acted upon, resulting in cellular disorder, with its expulsion from the cell, thus hyperglycemia and glycosauria. Tyroxine is dissociated into tyrosine and iodine. The absence of tyrosine leads to a change in patient's temparament. Adrenalin controls the electrolytes, while its absence causes undue fatigue. Cholesterol ester splits into cholesterol and fatty acids. The cholesterol radical acts as a transport agent, while fatty acids remain in the tissue fluids. The fatty acids ~~xxxxxxxxxxxx~~ are permitted to enter into the cytoplasm of the cell and take its place around Golgi apparatus, through the process of chemotropism. Siderophillin gives up its iron. Hemoglobin of the red blood cell gives up its oxygen, while the erythrocyte remains as a transport agent.

The vitamin -B factors are dissociated into pyridoxine, niacinamide, riboflavin, nicotinic acid, panthothenic acid, thiamine hydrochloride and biotin, which on entering the cytoplasm of the cell are reassembled by the genes to form the potential link of the prosthetic group of the coenzyme system. As a whole, vitamins play an essential role in cellular metabolism, for the lack in any particular vitamin reduces the rate of the metabolic process, leading to specific deficiency diseases. e.g. Vitamin-A, under the direct influence of the gene unites with a special amino acid facilitiated by a mineral to form a prosthetic group or visual purple, which directs specific chemical reaction. Visual purple is found in the rods of the retina of the eye, chemically changed and bleached by light, the change being the bases of functions of rods as light sensitive receptors, increased in amount in dark, raising sensibility of rods to faint light."

A defect in gene-constitution, or an interference with its activities fail to assemble the prosthetic coenzyme system or visual purple leading to night-blindness. Similarly, the lack of vitamin-C leads to scurvy, vitamin-D causes rickets, vitamin -E abortions and sterility in men, vitamin-K causes proneness to bleeding. Menadione gives up vitamin -K, while vitamin -12 is associated with cobalt.

A normal osmotic pressure is established and these components are selectively and continually permitted to enter the cytoplasm of cells becoming utilisible for cellular metabolism. Cellullar metabolism depends upon the normal pH, a temperature that is isothermal and unified action of the enzymic components, which are driven to activityby such minerals as iron, iodine, cobalt, copper, and magnesium. "Upon the physico-chemical state of this organic medium in which the cells live depends not only our health but even th manifestation of our psychic life,our very thoughts and emotions."

cell chromosomes and displays greater variety in rapid growth. This idea follows the second law of thermodynamics 'which expresses in precise, mathematical form the fact that all things, atoms included, are constantly tending to go in a state of maximum disorder and that to reverse this process involves the expenditure of energy.' The utilization of this intercellular energy leads to chemical differentiation while entropy results in lack of differentiation as exhibited in the cancer cell. Finally, the subsequent division of these cells depends upon the time period in which they were isolated i.e. the more embryonal the cell, the more multiplying the cell, the more malignant the tumor.

SENESCENCE

It was once suggested that cancer is a disease of old age where the inevitable consequence of the body degeneration resulted in senescence and the transformation of cells of adult complexity to dividing cells, the so-called metaplasia. Metaplasia has been defined as, "the change of one kind of tissue into another also the production of tissue by cells which normally produce tissue of another sort." The metaplasia theory which describes dividing cells in an environment of adult complexity would then accept the ~~them~~ concept of the reversibility and irreversibility of differentiation. This concept must be regarded as a philosophic rather than a biologic catena, since embryologists tell us that once the cell has been committed to a certain type of differentiation it cannot change to any other type.

(b) The genes, the bearers of heredity, would not permit such a change or, if it were possible, it would reproduce like by like ~~since genes are facsimile.~~

cells convey to a new generation

adulthood but, in a strict sense, a true steady state is never achieved, but is approached more and more slowly as life proceeds. This may be seen in the gradual decrease in basal metabolism and in other physiological characteristics which change with age."

Thus every cell, tissue or organ may have its particular response in a gradual decrease in basal metabolism and in other physiological characteristics which change with the period which ushers in the phase of senescence, or in the words of William Shakespeare in As You Like It:

"Last scene of all,
That ends this strange eventful history,
Is second childishness, and mere oblivion
Sans teeth, sans eyes, sans taste, sans everything."

For example the skin reaches its biological true terminus and the basal cells can no longer act as an organ of physiological regeneration, as evidenced by atrophy, anesthesia and dehydration. While individual cells representing "reserve elements" may resume to grow and multiply according to their kind to produce dividing cells in an environment of adult complexity.

Since the skin has been the object of both clinical and experimental observation in

Histologically there is no response to the tissue ~~to the~~ irritation, such as hyperplasia, acanthosis & papillary projections characteristic of psoriasis

mechanism of the cancer process it may be used as an illustration. Embryologically the single-layered ectoderm proliferates cells which change their form or structure to produce layers of the epidermis sweat glands, mammary glands, salivary glands, and mucous glands which become the cells of adult complexity. The ectoderm, through histogenetic differentiation becomes a stratified-squamous epithelium as follows: The basal cells remain in a state of potential, rather than actual function, often with active division ~~[illegible], the final act of the skin and other~~ but as their ultimate function is in fact already fixed, they must be considered as differentiated. During this process of physiological regeneration ~~this~~ desoxyribonucleic acidises desoxyribonucleic acid into hypo-xanthine, xanthine, uric acid & urea as these cells move up to the surface to become precornified, cornified and keratinized. Histologically, the basal cell and its immediate descendants are recognized, that is, stratum germinativum, stratum granulosum, stratum lucidum, and stratum corneum. The resulting keratinized cells diminish water loss, cut off rays of the sun, and prevent the entrance of pathogenic bacteria and are subsequently eliminated as dead cells.

~~(Chart~~

~~Vertical section of Epidermis & papillae of Corium~~: The physiological growth of squamous epithelium is characterized by two attributes:-

(1) a marked tendency to proliferation
(2) tendency to surface growth - protective epithelium.

Under this protective layer is a thicker dermis or corium, a derivative of somatic mesoderm. This layer passes through chemical differentiation to become the basal connective tissue which proliferates fibroblasts, fibrocytes, and collagen fibres, giving the epidermis its mechanical strength. Histologically, this layer, consists of the basal connective tissue in which fibroblasts fibrocytes, macrophages, intracellular material, blood vessels, collagen fibers, nerve fibres and sweat glands with ducts can be recognized. CHART (Page 2) cont.

Subject this layer in the presence of a cancer cells or tumor of isolation to an irritant which is mild, prolonged and of definite intensity and interpret the cell-like mechanism. The action of the irritant is greatly influenced by the cells with which it comes in contact and they respond in the characteristic fashion that may be described in the following phases (a) the prenatural phase

(b) induction phase, (C) initiation of the cancer process.

A. Promotional phase (1) response of the tissue to the irritant etc (fill in from typed script) of page 43. (elaborate) Vide Chart p10

(2) Response of injured cells to the irritant: Injured cells, through the forces of mobilization, liberate local metabolites, i.e. they cause the splitting of carbon dioxide from histidine & liberating histamine. The toxic histamine then dilates capillaries, veins, and arterioles, bringing in an increased amount of blood flow resulting in redness heat edema and a reactive hyperemia. Leukotaxin increases the permeability of the walls of the blood vessels and permits the escape of intracellular proteins, water electrolytes, androgenic or estrogenic hormones, vitamins B_{12} and folic acid, purine & pyrimidine bases, insulin, thyroxin, cholesterol esters, siderophilin & oxygen etc to cause the swelling. These components are dissociated into simpler blocks adhering to one of the oldest principles of physiology: "Corpora non agunt nisi soluta" (Substances do not act or wander unless dissolved.) " This area of inflammation becomes more or less isolated from the rest of the organism, developing its own hydrogen-ion concentration, its own circulation and

TISSUE FLUIDS AND A CELL

CAPILLARY DEPOSITS

RED BLOOD CELL, OXYGEN
Glycogen, Gluco-6-phosphate
Cholesterol Esters, Fatty Acids, Cholesterol.

Polypeptides.
- Arginine
- Histidine,
- Lysine
- Valine
- Proline
- Tyrosine
- Phenylalanine

Endipermable (red)

Purine Bases
- Adenine
- Guanine

Pyrimidine Bases
- Cystosine
- Uracil
- 5 methyl-cystosine
- Thymine

Androgenic & Estrogenic Hormones
- Cholesterol Radical
- Amino Acid.

Vitamin -B Factors.
- Riboflavine
- Thiamine Hydrochloride
- Pyridoxine
- Nicotinamide
- Biotin.

Insulin, Zinc, Sulphydril Group

Thyroxine, Iodine, Tyrosine.

Siderophillin, Iron.

Adrenalin

PhosphoricACID

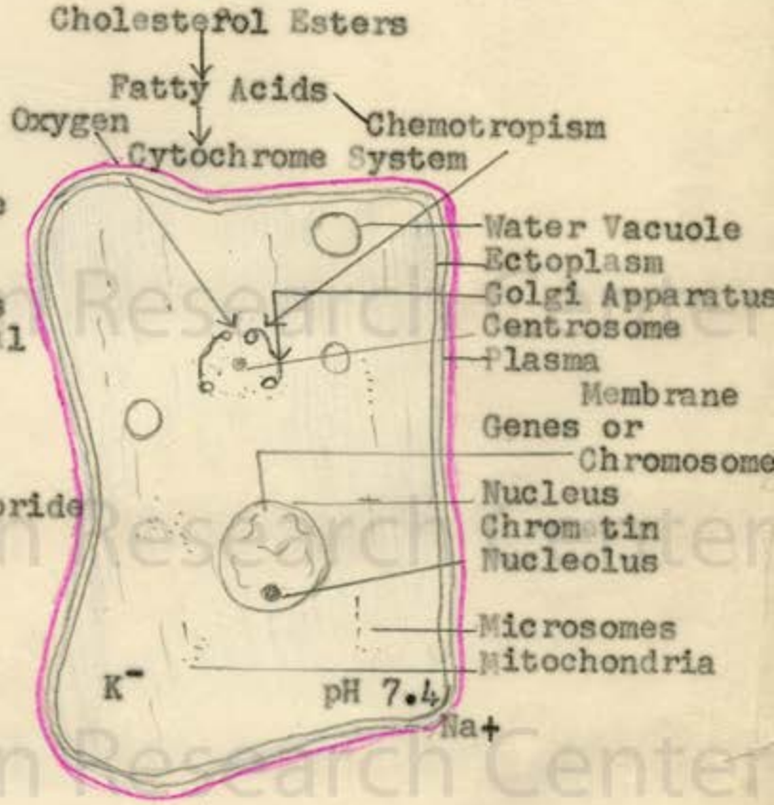
Vitamin A, C, D, E.

Menadione

Vitamin K

Minerals,
- Calcium,
- Cobalt,
- Copper,
- Magnesium,
- Manganese,
- Molybdenum.

Vitamin B 12.



GOLGI APPARATUS

Androgenic and estrogenic esters split into amino acids and cholesterol radical, the amino acid of the hormone acts as a transport agent, while the cholesterol radical bedomes the organiser of the embryonal tissue, and initiator of both the cell of adult complexity and the cancer cell. Insulin splits into reactive cystine and zinc, sulhydryl group, acting as a transport agent, while the zinc on entering the cytoplasm of the cell, becomes a potential link of the coenzyme system for CBHT metabolism, i.e. glycogen is broken by hexokinase into gluco-6-phosphate as it enters the tissue fluids. Gluco-6-phosphate is then permitted to enter the cytoplasm of the cell by the plasma membrane, and ferments into pyruvic acid. Zinc unites with a special amino acid and vitamin to establish a prosthetic coenzyme system, which automatically directs specific chemical reaction. Pyruvic acid, under this calalytic system and oxygen pass through nine successive reactions, liberating CO_2 and H_2O and energy after each reaction, thus making each step-stage rection possible. Zinc also"forms the prosthetic group of the enzyme carbonic anhydrase and plays an important part in the transport of CO_2 by the blood". On elimination, zinc frees itself from CO_2 and may be taken back by the blood to the Islets of Langerhan, where it is resynthesised into reactive cystine or insulin. Insulin is again taken by the blood to the tissue fluid dissociates into sulhydril group and zinc, where it is again permitted to enter into the cytoplasm of the cell by the plasma membrane to be reassembled by the genes as a prosthetic group for CBHT metabolism. Thus the reversibility and the irreversibility of Zinc metabolism. The absence of insulin causes Diabetes Mellitus, i.e. the absence of zinc, which usually forms a prosthetic system. Entropy is sestablished, i.e. energy that is not